A new tool to prevent malaria shows promise: Antibody drugs

By Carolyn Y. Johnson October 31, 2022 WP

Kassoum Kayentao, one of the leaders of a trial that found an antibody treatment could prevent malaria, explained the research to community leaders and residents in Kalifabougou, Mali. (Peter Crompton/National Institutes of Health)

A single dose of an antibody drug provided strong protection against malaria infections during the six-month rainy season in Mali, an international team of researchers announced Monday. The promising result, published in the New England Journal of Medicine, lays the groundwork for a new tool to help defeat a parasitic disease that last year killed more than 600,000 people — mostly children. The experimental drug, CIS43LS, proved 88 percent effective in preventing malaria infections in healthy adults — a tantalizing proof of principle that such an approach could have a powerful impact.

“This is extremely good, particularly when considering that the study was implemented in an area of intense seasonal transmission,” Umberto D’Alessandro, a malaria expert at the London School of Hygiene and Tropical Medicine based in Gambia, said in an email. He was not involved in the study.

But it represents a first step, not a final product. The drug is given to recipients in a 30-minute intravenous infusion that would be impractical to widely implement, and another drug following behind it that is more potent and easier to administer is more likely to enter the final stages of development. An antibody drug would be one tool, not a single solution, to fight malaria.

The study opens up a whole new class of drugs to tackle malaria, a disease that is caused by a parasite in the saliva of infected mosquitoes. A team at the National Institutes of Health isolated a parasite-blocking antibody from the blood of a volunteer who was given an experimental malaria vaccine, then tweaked the antibody so that it would stick around in the blood and offer protection for months at a time.

The NIH team — partnering with researchers at the Mali International Center for Excellence in Research, which is at the University of Sciences, Techniques and Technologies of Bamako, Mali — subjected the drug to an intense test for malaria prevention: the rainy season. That period begins in June, with transmission peaking in October.

In the rural Malian villages where the researchers work, young children on average experience two potentially life-threatening malaria infections in a single season, but can suffer as many as five.

In the study, 330 healthy adults received either a high dose of CIS43LS, a low dose, or a placebo. The high dose was 88 percent effective and was more likely to cause moderate headaches. The lower dose was 75 percent effective in preventing infection.

A constellation of approaches exist in the quest to prevent malaria: insecticide-treated bed nets, oral anti-malarial drugs that are given to children and pregnant women, and a vaccine that was recently approved by the World Health Organization. Still, Kassoum Kayentao, one of the leaders of the clinical trial, said there is a need to build a bigger and more effective arsenal against malaria.

“The monoclonal that we are discussing right now provides immediate protection after a single shot, for about six months,” Kayentao said. “It could help complement the existing tools.”

Already, a similar, second-generation antibody drug developed at NIH is being tested in children in Mali and Kenya. That drug could be more practical if proven effective because it requires a lower dose. The trials are conducted in healthy adults initially, but the ultimate impact will need to be measured in children or pregnant women who are most vulnerable to malaria.

Robert Seder, chief of the cellular immunology section at the National Institute of Allergy and Infectious Diseases, said he and his team began working on the second-generation antibody, called L9LS, nearly in tandem with the first version. They knew that a more potent drug could reduce the cost and ease the administration — crucial improvements if the drug is going to be practical to use in countries where malaria is endemic.

"If … we need something a little more potent, or that has a better half-life, I have a third-generation antibody we're looking at now," Seder said. "You never stop."

Researchers are just beginning to debate how an antibody drug — they have traditionally been expensive to manufacture — could be used in combination with other tools.

To control outbreaks, a monoclonal antibody could provide an instant dose of protection. It might be useful in protecting seasonal workers or travelers in some regions. It could be used in combination with a vaccine to provide a higher level of protection. A dose that could protect a woman and her fetus through a pregnancy could be powerful. And people who are immunocompromised and do not respond well to vaccination could benefit.

"I'm excited about this," said Johanna P. Daily, a professor of microbiology and immunology at Albert Einstein College of Medicine, who was not involved in the research. She added that every anti-malaria tool might have a different strength and use.

"If we have the vaccine, and we have the monoclonals, and we have preventive drugs, every region has different transmission levels — they may have to figure out their own special cocktail," Daily said.

The results are "very exciting and very promising," said Jacqueline Kirchner, a senior program officer at the Bill & Melinda Gates Foundation, which is co-funding the follow-up study in Kenya. "This is a major new innovation that could save lives, address growing drug resistance and ultimately accelerate — along with these other tools — the eradication" of the malaria parasite.

A malaria vaccine was endorsed by WHO last year, a major milestone for public health. Still, that vaccine left more work to be done to save lives.

The vaccine, RTS,S/AS01, is 30 percent effective in preventing deadly severe malaria in children — an important advance, but one that can be most powerful when combined with other prevention methods. An experimental vaccine in development, R21/Matrix-M, has been shown to be 78 percent effective in children in Burkina Faso after three doses plus a booster.

Peter D. Crompton, chief of the Malaria Infection Biology and Immunity Unit at NIH, said he and Kayentao are already planning a trial in 2024 to compare the monoclonal antibody to a pill regimen used in children in areas where malaria

transmission is seasonal. The pills can be effective, but must be taken multiple times during a season.

“If you ask any malaria researcher: What would be the ideal tool? It’s a vaccine that delivers high-level protection for a very long time. One, two, three visits, and you’ve protected a kid” long term, Crompton said. “Unfortunately, we’re not there, and most of us think we’re not anywhere close to that. We’re looking to fill the gaps, and right now, the gaps are many. A tool like a monoclonal … could have a role.”